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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/559,610	FILICORI, MARCO	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,8,11-13,16-19,34,37,45-47,50 and 51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7,8,11-13,16-19,34,37,45-47,50 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/19/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 19 March 2010 has been entered.

Status of Application, Amendments and/or Claims

The amendment and Applicant's arguments, filed 19 March 2010, have been entered in full. Claims 1, 34, 45, 46, 47 are amended. New claims 50 and 51 are added. Claims 2-6, 9, 10, 14, 15, 20-33, 35, 36, 38-44, 48 and 49 are canceled. Claims 1, 7, 8, 11-13, 16-19, 34, 37, 45-47, 50 and 51 are under examination.

Information Disclosure Statement

The information disclosure statement(s) (IDS) (filed 19 March 2010) was received and complies with the provisions of 37 CFR §§1.97, 1.98 and MPEP § 609. It has been placed in the application file and the information referred to therein has been considered as to the merits. It is noted that lined references which state "considered do not print" have been considered by the Examiner, but will not be printed on the face of the patent issuing from this application because they are not true publications.

Withdrawn Objections And/Or Rejections

The rejection to claims 1, 11-13 and 19 under 35 U.S.C. 102(b) as being anticipated by Filicori et al. (Fertility and Sterility, Vol. 72, No. 6, Dec. 1999), as set forth at pages 4-5 of the previous Office Action (21 September 2009), is *withdrawn* in view of the amendment (19 March 2010).

The rejection to claims 1, 11, 13, 16 and 19 under 35 U.S.C. 102(b) as being anticipated by Thompson et al. (Fertility and Sterility, Vol. 63, No. 2, Feb 1995), as set forth at pages 5-6 of the previous Office Action (21 September 2009), is *withdrawn* in view of the amendment (19 March 2010).

The rejection to claims 1, 7, 8, 11, 13, 16 and 19 under 35 U.S.C. 102(b) as being anticipated by Menezo (WO 03/022303 A2), as set forth at pages 6-7 of the previous Office Action (21 September 2009), is *withdrawn* in view of the amendment (19 March 2010).

The rejection to claims 17 and 18 under 35 U.S.C. 103(a) as being unpatentable over Menezo (WO 03/022303 A2) as applied to claims 1 and 16, and further in view of Skrabanja et al. (US Patent 5,929,028), as set forth at pages 7-9 of the previous Office Action (21 September 2009), is *withdrawn* in view of the amendment (19 March 2010).

Claim Rejections-35 USC § 102(b)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 45 remains rejected under 35 U.S.C. 102(b) as being anticipated by Skrabanja et al. (reference of record; US Patent No. 5,929,028). The basis for this rejection is set forth at page 7 of the previous Office Action (21 September 2009).

Skrabanja et al. teach a method of treating infertility by the administration of gonadotropins (column 50-57). Skrabanja et al. teach gonadotropin-containing formulations comprising FSH or hCG or mixtures thereof (abstract; column 3, lines 15-26; column 3, lines 59-65; column 4, lines 22-30). Skrabanja et al. teach methods of admixing in an aqueous solution at least one gonadotropin (column 5, lines 62-67). Skrabanja et al. teach that FSH doses ranges from about 25 to 1500 IU, especially 5-225. Skrabanja et al. teach that as high as 10,000 IU and as low as 15 IU of hCG have been administered. Skrabanja et al. teach that suitable concentrations of FSH ranges from about 20-2000 IU/ml, which roughly corresponds with a concentration of 2-200 ug/ml (column 6, lines 23-41)**(applies to claim 45)**.

Applicant argues that claim 45 is directed to a single product comprising a first pharmaceutical composition comprising recombinant FSH and a second pharmaceutical composition comprising recombinant hCG, wherein the amount of recombinant hCG in the second pharmaceutical composition is about 0.1 ug to about 2,000 mg/ml. Applicant argues that Skrabanja et al. does not teach such a product. Applicant agues that while Skrabanja teaches compositions that comprise FSH or hCG or both in admixture, Skrabanja does not teach or suggest a single product that comprises two separate compositions, one comprising recombinant FSH and the other recombinant hCG. Applicant argues that although Skrabanja mentions that FSH and hCG can be dissolved

together, this teaching does not relate to single, multi-component product as recited in claim 45.

Contrary to Applicant's assertion, the instant claim recites, "..wherein the amount of **recombinant FSH in the first pharmaceutical composition** is from about 0.1 ug to about 2,000 mg/ml. Secondly, the instant claim **does not** recite, "..a single product that comprises two separate vials (wherein the first vial comprises FSH and the second vial comprises hCG). The instant claim is drawn to a single product comprising two compositions. ***Furthermore*, claim 9 of Skrabanja et al. recite a Markush group of gonadotropins and mixtures thereof.** Thus, Skrabanja et al. teach a cartridge comprising FSH with stabilizing amounts of polycarboxylic acid **AND** a cartridge comprising hCG with stabilizing amounts of polycarboxylic acid **OR** a cartridge comprising a mixture of FSH and hCG with stabilizing amounts of polycarboxylic acid. See also column 3, lines 15-20; column 3, lines 50-65 and column 6, lines 42-46. Skrabanja et al. teach that the invention relates to a liquid gonadotropin-containing formulation which comprises a gonadotropin and stabilizing amounts of a polycarboxylic acid or a salt thereof (column 3, lines 15-20). Skrabanja et al. teach that the gonadotropin or gonadotropin derivatives, as used in the definition of the formulation of the present invention, are follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), human chorionic gonadotropin (hCG), luteinizing hormone (LH), or derivatives, or analogs, and mixtures thereof, with or without other protein components (column 3, lines 50-65). Skrabanja et al. teach that in one preferred embodiment, a combination of FSH and hCG are dissolved together to form a formulation (column 6,

lines 42-46). The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Rejections-35 USC § 102(e)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 34, 45-47 remain rejected under 35 U.S.C. 102(e) as being anticipated by Sharma et al., United States Patent Application Publication US 2003/0181361. The basis for this rejection is set forth at page 7 of the previous Office Action (21 September 2009).

Sharma et al. teach pharmaceutical formulations comprising therapeutic proteins and polymers (abstract and para 0001). Sharma et al. teach that due to recent advances in genetic and cell engineering technologies, proteins known to exhibit various actions *in vivo* are capable of production in large amounts for pharmaceutical applications (para 0002). Sharma et al. teach that the invention provides a method to prepare aqueous sustain-release pharmaceutical formulations of therapeutic proteins for parenteral administration (para 0011). Sharma et al. teach protein expression and purification (0034). Sharma et al. teach formulations wherein the protein is selected from the group consisting of FSH and hCG (paras 0047, 0055 and claim 13). Sharma et

al. teach that the formulation will contain about 1 ug/ml to about 2000 ug/ml of protein per formulation (para 0036)**(applies to claims 34, 45-47)**.

Applicant argues that Sharma does not teach the products recited in claims 34, 46 and 47. Applicant contends that Sharma focuses on erythropoietin, but also lists many possible recombinant proteins to be formulated in accordance with its technology. Applicant maintains that Sharma's broad disclosure of numerous possible recombinant proteins recited in the claims would not have led the skilled artisan to compositions comprising the specific proteins recited in the claims, in the amounts recited in the claims. Applicant argues that Sharma does not teach or suggest a single product comprising both an FSH composition and an hCG composition.

Applicant's arguments have been fully considered but are not found persuasive. The Examiner notes that claims 34, 37, 45, 46 and 47 are all drawn to a single product comprising a first pharmaceutical composition comprising FSH and a second pharmaceutical composition comprising hCG. **The Examiner notes that Applicant argued Skrabanja did not teach or suggest a single product that comprises two separate compositions, one comprising recombinant FSH and the other recombinant hCG** (rejection to instant claim 45). Now Applicant argues that Sharma **does not teach or suggest a single product comprising both an FSH composition and an hCG composition** (rejection to instant claims 34, 46 and 47). *Please see the 112, Second Paragraph rejection below.*

The instant claims are drawn to a single product comprising two compositions. Sharma et al. clearly teach a pharmaceutical formulation wherein the protein is selected

from the group consisting of FSH and hCG (para 0055 and claim 13). **Claim 13 of Sharma et al. recite a Markush group of gonadotropins.** Thus, Sharma et al. teach a pharmaceutical formulation comprising FSH **AND** a pharmaceutical formulation comprising hCG. Sharma et al. teach protein amounts from about 1 ug/ml to about 2000 ug/ml (para 0036). Sharma et al. anticipates the instant claims. Lastly, in response to Applicant's argument that Sharma focuses on erythropoietin, but also lists many possible recombinant proteins to be formulated in accordance with its technology, MPEP 2131.02 states a genus does not always anticipate a claim to a species within the genus. However, when the species is clearly named, the species is anticipated no matter how many others are additionally named. Ex parte A, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990). The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Rejections-35 USC § 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 37 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Sharma et al. as applied to claim 34 above, and further in view of Skrabanja et al. (reference of record; US Patent No. 5,929,028). The basis for this rejection is set forth at pages 12-13 of the previous Office Action (21 September 2009).

The teachings of Sharma et al. are described above. Sharma et al. do not teach formulations further comprising a syringe. Skrabanja et al. teach gonadotropin-containing formulations comprising FSH and hCG or mixtures thereof (abstract; column 3, lines 15-26; column 3, lines 59-65; column 4, lines 22-30). Skrabanja et al. teach a device for administration comprising a cartridge containing a sterile liquid formulation according to the invention. Skrabanja et al. teach that a preferred device for administration is a pen-type injector. Skrabanja et al. state that using an injector with a suitable scale indication, the patient can simply inject each time the quantity needed. (column 6, line 56-column 7, line 25).

It would be obvious to one of skill in the art at the time the invention was made to modify the aqueous sustain-release pharmaceutical formulation of therapeutic proteins for parenteral administration comprising recombinant FSH and recombinant hCG as taught by Sharma et al. by formulating it to further comprise an injection device (i.e. syringe) as taught by Skrabanja et al. with a reasonable expectation of success. The motivation and expected success is provided by Sharma and Skrabanja, who both teach aqueous formulations comprising recombinant FSH and recombinant hCG. Because Sharma et al. teach parenteral administration of FSH and hCG, it would be obvious to supply a device to inject the pharmaceutical.

Applicant argues that Sharma does not teach a product according to claim 34 and that combining Sharma and Skrabanja does not render obvious the embodiments recited in claim 37. Applicant emphasizes that neither Sharma nor Skrabanja (alone or in combination) teach or suggest a pharmaceutical composition comprising recombinant

hCG in the amounts recited in claim 34. Applicant maintains that neither Sharma nor Skrabanja (alone or in combination) teach or suggest a single product comprising both recombinant FSH composition and hCG composition.

Applicant's arguments have been fully considered but are not found persuasive. As was stated above, the instant claims are drawn to a single product comprising two compositions. Sharma et al. clearly teach a pharmaceutical formulation wherein the protein is selected from the group consisting of FSH and hCG (para 0055 and claim 13). Sharma et al. clearly teach protein amounts from about 1 ug/ml to about 2000 ug/ml (para 0036). Skrabanja et al. teach syringes. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d `1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 7, 8, 11-13, 16-19 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of **copending Application No. 11/898,470.** The basis for this rejection is set forth at pages 9-10 of the previous Office Action (21 September 2009). Applicant states that the instant applications both are still undergoing active prosecution. Applicant defers addressing the rejections on their merits until one or more of the applications are otherwise in condition for allowance. The instant rejection is maintained for reasons of record.

Claims 1, 7, 8, 11 and 13 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of **copending Application No. 11/979,265.** The basis for this rejection is set forth at pages 9-10 of the previous Office Action (21 September 2009). Applicant states that the instant applications both are still undergoing active prosecution. Applicant defers addressing the rejections on their merits until one or more of the applications are otherwise in condition for allowance. The instant rejection is maintained for reasons of record.

NEW CLAIM REJECTIONS/OBJECTIONS

Claim Rejections - 35 USC § 102(b)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 7, 8, 11-13, 16-19, 50 and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Franks et al. (Reference of record; WO 00/67778).

Franks et al. teach that the present invention relates to the use of gonadotropins in the induction of folliculogenesis. Franks et al. teach the use of luteinizing hormone; LH (or an equivalent dosage of human chorionic gonadotropin hCG) in the production of a medicament for inducing folliculogenesis (abstract). **Franks et al. teach the use of LH in the production of a medicament in a range from 100 to 1500 IU; 200 to 800 IU; 225 to 450 IU** (page 4, lines 25-30 and page 5, lines 7-19). **Franks et al. teach that FSH may be used in the medicament.** Franks et al. teach that the IU ratio of LH to FSH is preferable in the range of from 1.5: to 20:1; 1.5:1 to 10:1 (page 7, lines 5-20 and page 8, lines 1-8). **Franks et al. teach that LH may be replaced by an equivalent dose of hCG. Franks et al. teach that an equivalent dose of hCG is calculated on the basis that 1 IU of hCG is equivalent to 5-7 IU of LH in the pharmacopaeia Van Hell bioassay** (page 7, lines 24-30). Based on the teachings of Franks et al., 150 IU of LH in a 2:1 ratio with FSH would equal 150 IU of LH and 75 IU of FSH and be equivalent to *75 IU FSH and 25 IU hCG*. 500 IU of LH in a 10:1 ratio with FSH would equal 500 IU of LH and 50 IU of FSH and be equivalent to *50 IU FSH and 100 IU hCG* (**applies to claims 1, 7, 8, 19 and 50**). Franks et al. teach that LH, FSH and hCG may be obtained from natural sources, e.g. isolated from urine, pituitary or placenta, or may be obtained using recombinant DNA technology (page 8, lines 20-

25)(**applies to claim 11**). Franks et al. teach that the formulation may be presented in unit-dose or multi-dose containers, ampoules and vials. Franks et al. teach that the medicaments can be lyophilized. Formulations can be administered through prefilled syringes (page 9)(**applies to claims 12, 13, 16-19 and 51**).

Claim Rejections -35 USC § 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 11-13, 16-18, 50 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Filicori et al. (Reference of record; Fertility and Sterility, Vol. 72, No. 6, Dec. 1999) in view of Skrabanja et al. (reference of record; US Patent No. 5,929,028).

Filicori et al. teach the administration of 75-150 IU FSH with 50 IU hCG to induce folliculogenesis (abstract and page 1119, 4th full paragraph and page 1120)(**applies to claim 1**). Filicori et al. teach that the FSH is the brand name Metrodin and that hCG is the brand name Profasi (page 1119, 3rd full paragraph). Metrodin is taught as a gonadrotropin extracted from the urine of postmenopausal women comprising FSH which is produced in a lyophilized form (Reference of record; Appendix A). Profasi is taught as a gonadotropin extracted from the urine of postmenopausal women which is produced in a lyophilized form (Reference of record; Appendix B) (**applies to claims**

11-13). Because FSH and hCG was administered to patients via injection, it must be in liquid form at some point (**applies to claims 16 and 17**). Filicori et al. do not teach a single injectable formulation comprising FSH and hCG. Filicori et al. do not teach said formulation supplied in pre-filled syringes or cartridges.

Skrabanja et al. teach that their invention resides in a method of treating infertility by the administration of gonadotropins (column 50-57). Skrabanja et al. teach gonadotropin-containing formulations comprising FSH or hCG or mixtures thereof (abstract; column 3, lines 15-26; column 3, lines 59-65; column 4, lines 22-30). Skrabanja et al. teach that the formulation may be supplied in cartridges, ampoule, vials, bottles or bags and that the cartridge may contain an amount of the liquid gonadotropin formulation corresponding to one or more therapeutic dosages (column 6, lines 56-67 and claims).

It would be obvious to one of skill in the art at the time the invention was made to modify 75-150 IU FSH and 50 IU hCG, used to induce folliculogenesis, as taught by Filicori et al. by formulating it as a single composition and supplying the pharmaceutical in pre-filled syringes or cartridges as taught by Skrabanja et al. with a reasonable expectation of success. The motivation and expected success is provided by Filicori and Skrabanja. Filicori et al. states that **the concomitant administration of low dose hCG and FSH** markedly reduced the duration of treatment (abstract and page 1120 3rd and last paragraph). Because Filicori et al. teach parenteral administration of FSH and hCG, it would be obvious to supply the formulation is devices to inject the drug, as taught by Skrabanja et al.

Claims 1, 11, 13, 16-18, 50 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Menezo (Reference of record; WO 03/022303 A2) in view of Skrabanja et al. (reference of record; US Patent No. 5,929,028).

Menezo teaches methods of administering gonadotropins for improved implantation rates (page 3, lines 30-37). Menezo teach the **use of hCG in conjunction with controlled ovarian hyperstimulation (COH) in human patients using FSH** (page 4 and page 6, lines 31-35). Menezo teaches where hCG is used in conjunction with COH using FSH, administration of hCG should preferably not be started until at least 3 days after beginning FSH treatment, for example between the 3rd and 10th day after starting FSH (page 7, lines 26-36). Menezo teaches 75-200 FSH/day or 150 IU FSH/day. Menezo teaches 25-1000 IU hCG/day or 50-100 IU of hCG/day (page 5)(**applies to claim 1**). Menezo et al. teach that when hCG is used in the aspects of the invention, the dosage should be in the range of 25-4000 IU, preferable 25-1000, more preferably 30-1000 or 30-500 IU and particularly preferably 50-100 IU or 75-125 or 75-100 IU or 75 or 100 or 500 or 75 or 100 to 1000 IU (page 8, lines 24-31 and page 9, lines 21-35). Menezo et al. teach that aspects of the invention are used in conjunction with COH regimens; FSH may be administered at or about 75 to 250 or 75 to 200 IU, preferably at or about 150 to 200 IU (page 11, lines 5-20) (**applies to claim 1**). Menezo teaches the use of urinary or recombinant hCG (page 16, lines 1-5). Menezo teaches the use of urinary or recombinant FSH (page 18, lines 1-9)(**applies to claim 11**). Because FSH and hCG is administered to patients via injection, it must be in liquid form at some point (**applies claim 16**). Menezo teaches a kit comprising doses of FSH and

hCG (Menezo; claim 24). Menezo does not teach said formulation supplied in pre-filled syringes or cartridges.

Skrabanja et al. teach that their invention resides in a method of treating infertility by the administration of gonadotropins (column 50-57). Skrabanja et al. teach gonadotropin-containing formulations comprising FSH or hCG or mixtures thereof (abstract; column 3, lines 15-26; column 3, lines 59-65; column 4, lines 22-30). Skrabanja et al. teach that the formulation may be supplied in cartridges, ampoule, vials, bottles or bags and that the cartridge may contain an amount of the liquid gonadotropin formulation corresponding to one or more therapeutic dosages (column 6, lines 56-67 and claims).

It would be obvious to one of skill in the art at the time the invention was made to modify 75-200 FSH/day or 150 IU FSH/day and 25-1000 IU hCG/day or 50-100 IU of hCG/day or 75-100 IU hCG/day, to improve embryo implantation rates, as taught by Menezo, by formulating it as a composition and supplying the pharmaceutical in pre-filled syringes or cartridges as taught by Skrabanja et al. with a reasonable expectation of success. The motivation and expected success is provided by Menezo and Skrabanja. Menezo teach the use of low doses of hCG in conjunction with controlled ovarian hyperstimulation (COH) in human patients using FSH to aid in implantation of an embryo. Because Menezo teaches parenteral administration of FSH and hCG, it would be obvious to supply the formulation in devices to inject the drug, as taught by Skrabanja et al.

Applicant argues that Menezo describes administering FSH and hCG at different time points, often on different days and according to different administration regimes, thereby requiring separate compositions. Applicant argues that the kits defined in Menezo include separate and different doses of FSH and hCG and different number of doses of FSH and hCG. Applicant argues that that Skrabanja is cited for teaching liquid forms of FSH and hCG and various doses of FSH and hCG dissolved together. Applicant cites case law. Applicant argues that although Skrabanja indicates that FSH and hCG can be provided in a single composition, Menezo provides no reason for making a single preparation comprising both FSH and hCG in the same composition. Applicant argues that the claimed compositions are designed to achieve ovulation induction without ovarian hyperstimulation. Applicant cites the instant specification (paragraphs 0020 and 0021). Applicant argues that Menezo is directed to methods for controlled ovarian hyperstimulation. Applicant argues that where, as here, the claimed invention yields unpredictable results, the obviousness rejection is not proper under KSR. Applicant reminds the Examiner that that unexpected results achieved by a claimed composition can overcome an obviousness rejection of composition claims. Applicant cites MPEP 2144.09.

Applicant's arguments have been considered but are not found persuasive. Applicant's citation of MPEP 2144.09 is not applicable. The MPEP 2144.09 [R-6] section teaches close structural similarity between chemical compounds (homologous, analogues, isomers). Rejection based on close structural similarity founded on the expectation that compounds similar in structure will have similar properties. Such is the

not the case here; Menezo teaches *the exact amounts* of FSH and hCG cited in the instant claims. Menezo teaches 75-200 or 150 IU **FSH/day** and 25-1000 IU, 50-100 IU or 75-100 IU **hCG/day**. Menezo teaches that administration of hCG should preferably not be started until at least 3 days after beginning FSH treatment, for example between the 3rd and 10th day after starting FSH. In the Examples, Menezo teaches that at day 7, **the experimental group received 50-100 IU of hCG on a daily basis in combination with 150 IU of rFSH** (page 16). Contrary to Applicant's assertion, there are administration overlaps (i.e. where FSH and hCG are administered on the same day). Therefore it would be obvious to one skilled in the art to combine FSH and hCG for those days of overlap. Further, Skrabanja et al. was NOT cited because of its teachings of doses. Skrabanja et al. was cited because the reference teaches pre-filled syringes and cartridges. The reference also teaches that FSH and hCG can be mixed. It would be obvious to one skilled in the art to supply the formulation in devices to inject the drug. Lastly, Applicant's arguments regarding unpredictable results, obviousness and KSR are not found persuasive because there is factual basis in the record of 50-100 IU of hCG being administered in combination with 150 IU of FSH. There is no unpredictability regarding formulations comprising hCG and FSH, *as recited*. The instant claims read on a formulation comprising a mixture of FSH and hCG. Based on the teachings of Menezo, it would be obvious to combine those amounts of FSH and hCG as recited in the instant claims.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34, 37, 45, 46 and 47 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims are indefinite because based on Applicant's arguments, it is not clear if the claims encompass a product comprising a mixture of FSH and hCG or a product comprising two separate vials (wherein the first vial comprises FSH and the second vial comprises hCG). The metes and bounds of the instant claims cannot be determined. Clarification is requested.

Claim Objections

Claims 50 and 51 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 1 and 18. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). If the claims are not of similar scope, Applicant is asked to specifically point in the specification, the patentable distinction between the claims.

Conclusion

Claims 1, 7, 8, 11-13, 16-19, 34, 37, 45-47, 50 and 51 are rejected.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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6/2/10